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Background of the Establishment of a Control System for Human Embryo in the UK and Its Actual Function
— For the Construction of a Social Governance System of Life Science Technology in Japan —

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3.1 Introduction

"How should we handle human embryos?" (the early state of individual human development; an egg that starts development because of fertilization or nucleus transplantation), such a new question of bioethics was raised in association with the progress of life science technology. Particularly, recent rapid progress of life science technology has increased questions and expanded the region, and this is reflected by the situation in which guidelines notified by government organizations increased suddenly since 2001 (Table 1).

With such a background, at present when the time limit for reviewing the law of human cloning in 2004 is near at hand, how to handle human embryos is being discussed repeatedly by Council for Science and Technology Policy*1. Recently, establishment of embryonic stem (ES) cells from human embryo was started for regenerative medicine, and researches using human embryos have been increasingly demanded from the medical aspects of conquering diseases and disorders, and aging and dementia, as well as from the industrial aspect*2. The handling criteria have been decided not only in Japan but also in foreign countries, respectively, and amendment to the legal regulation was started with the change of the status after the regulation (Figure 1). For example, in Germany, where strict regulation on the use of human embryos was provided by law in 1991, use restricted to imported ES cells came to be permitted*3.

As for the actual situation in Japan, since the first child born by in vitro fertilization (IVF) in Japan in 1983, researches on assisted reproductive

Table 1: Bioethics-related laws and government policies in Japan

– Law No. 104 dated July 16, 1997 (Latest amendment: Law No. 160 dated Dec. 22, 1999) "Organ Transplantation Law" – Law No. 146 in 2000; December 2000 "The law concerning regulation relating to human cloning techniques and other similar techniques"
– Notification No. 1 of the Ministry of Health, Labour and Welfare, the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Economy, Trade and Industry in 2001; March 2001 " Ethical guidelines for research on human genome and gene analysis" – Notification No. 155 of the Ministry of Education, Culture, Sports, Science and Technology in 2001; September 2001 "The guidelines for derivation and utilization of human embryonic stem cells" – Notification No. 173 of the Ministry of Education, Culture, Sports, Science and Technology in 2001; December 2001 "The guidelines for handling of a specified embryo" (based on the law) – Notification No. 5 of the Ministry of Education, Culture, Sports, Science and Technology in 2002; January 2002 "The guidelines for recombinant DNA experiments" – Notification No. 1 of the Ministry of Education, Culture, Sports, Science and Technology, and Ministry of Health, Labor and Welfare in 2002; March 2002 "The guidelines for clinical research on gene therapy" – Notification No. 2 of the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labour and Welfare in 2002; June 2002 "Ethical guidelines for epidemiological research"

Figure 1: Comparison of the criteria for establishment of ES cells using human embryos and the use of ES cells among the countries (* shows a virtual placement)

Prohibition of establishment/ prohibition of use	Prohibition of establishment/ Permission of use of existing ES cells	Permission of use of embryos limited to surplus ones for establishment of ES cells	Permission of preparation of human embryo to establish ES cells, and permission of the use
Ireland, Norway, Switzerland, Poland, Italy*, Brazil, (10 states in USA (a))	Germeny (Jul 2002 and after), France* (May 2002 and after), Denmark, (Subject study of the US federal budget)	Japan, Korea, Russia*, Canada, Finland, Spain, Holland, Australia, (40 states* in USA (b))	UK, China, (40 states* in USA (b))

Acceptance of establishment of ES cells from cloned embryo
UK, China, State of California in USA

In the United States, the regulation and the virtual placement differ depending on the state. The states belonging to (a) are (i) Maine, (ii) Massachusetts, (iii) Rhode Island, (iv) Pennsylvania, (v) Florida, (vi) Michigan, (vii) Minnesota, (viii) North Dakota, (ix) Louisiana, and (x) South Dakota (prohibition of researches and imports of ES cells).
The State of Iowa prohibits cloning only. The states other than the above (i) to (x) virtually belong to (b). Unlike other 49 states, the State of California is said to accept researches of human embryos in almost the same way as the UK, and accepts establishment of ES cells from cloned embryo.

Source: Walters' data (2002) were modified, and some new information up to March 2003 was added.

medicine (reproductive medicine using ART for sterility therapy) have been conducted, including those associated with the preparation of embryos, for more than 20 years under the self-imposed regulation of the Japan Society of Obstetrics and Gynecology. In assisted reproductive medicine, there are surplus embryos (embryos fertilized *in vitro* that have lost their purpose of use for sterility therapy because a child was already born or for other reasons), but these are disposed of. On the other hand, as the restriction of ES cell research in regenerative medicine and embryology, creation of human embryos and use of human embryos are restricted by government policies, different regulations come to be applied to a single type of biological specimens, and ethical and social inconsistencies are indicated*[4].

As stated above, in the process of the development of current life science technology, resolution of the bioethical issue became a subject to be tackled by the society of each country as an essential process. That is, it came to be recognized that the practice of research activities was inseparable from the social acceptance of the researches*[5]. Such an inseparable relationship between life science technology and bioethics may be reflected in that the US allocates 3-5% of the national expenditure on genome researches for ethical, legal and social activities. Specifically, from 1990 to 1999, in the US, 58 million dollars (5%) from NIH and 18 million dollars (3%) from the Department of Energy were appropriated, resulting in the formation of an important intellectual foundation of bioethics-related policies (Ayano, 2001). The measures have raised the level of the ethics review board, etc., and allowed training of human resources to support them*[6].

As known well from the birth of the first IVF child in 1978*[7] and preparation of the cloned sheep in 1997*[8], the UK (United Kingdom) leads the world in the field of science technology. In addition, as for social control of human embryos, the UK has a unique social system with a history of one decade, having "the law, and the control organization designated by law" as the center of activity.

On the other hand, in Japan, is there any comprehensive social system that can act as a basis to dynamically adapt to the bioethical issue newly appearing and attempt to solve such issue? In order to solve the bioethical issue that is likely to become more serious in the future, under the current status we should consider the necessity of constructing a system (social governance system of life science technology) to combine life science technology and measures for social acceptance. At that time, the existing system in the UK would provide beneficial information to us. Therefore, I shall introduce the background of the control system of human embryos in the UK and the practical functions. Table 2 shows a comparison of regulations related to human embryos between the UK and Japan.

3.2 System consisting of laws and the control organization (see figure 2)

3.2.1 Traditional methods for deciding on the law

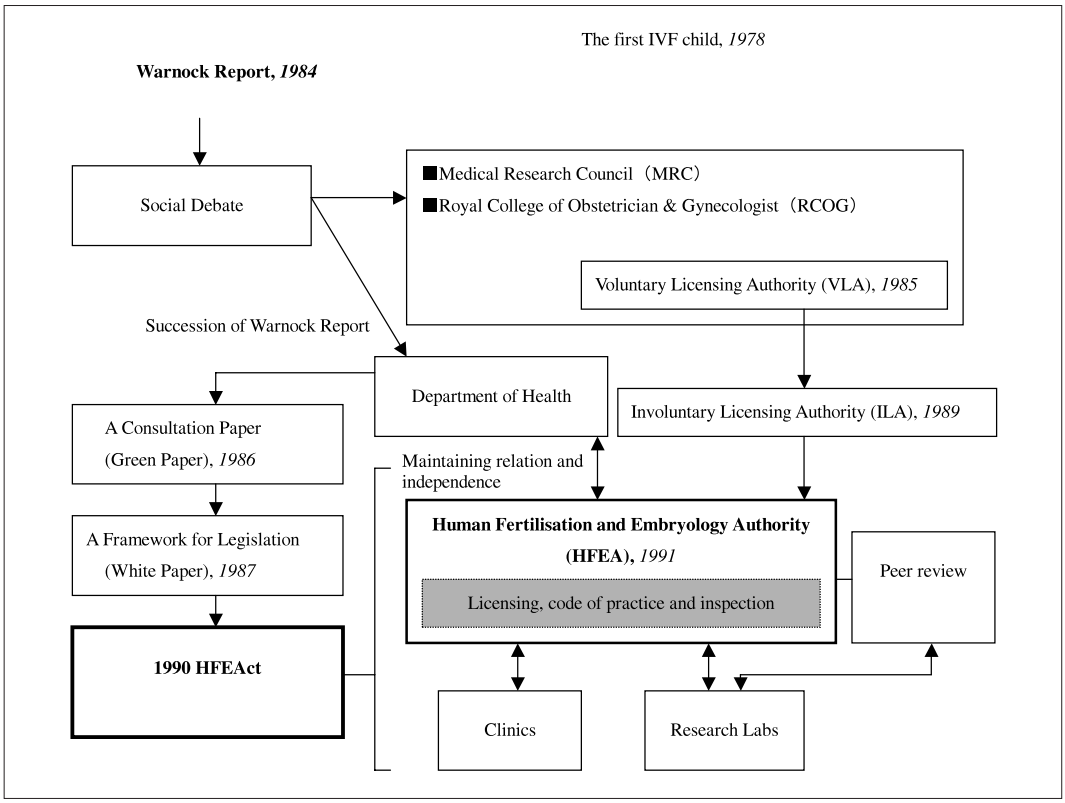
The control system of human embryos in the UK consists of the law and the special control

Table 2: Comparison of policies regarding human embryos between the UK and Japan

Compared item	UK	Japan
• Form of regulation	Law (Human fertilisation and embryology act, etc., in 1990)	Separate voluntary self-imposed controls by academic societies and the government.
• Control organization	License system by the special control organization (independent administrative committee)	Separate review system by academic societies and the government.
• Assisted reproductive medicine (preparation of in vitro fertilization embryo and transplant)	Allowed.	Allowed in the society's notice.
• Preparation of human embryo for researches	Allowed.	Allowed in the society's notice.
• Establishment of ES cells	Allowed.	Allowed for surplus embryos only by the government policy.
• Preparation of human embryo for establishment of ES cells	Allowed.	Prohibited by the government policy.
• Utilization of surplus embryos for research	Allowed.	Allowed in the society's notice.
Comparison of cloning policies • Form of cloning regulation	Law (Human reproductive cloning act in 2001)	Law (Cloning law * in 2001) and the guideline based on the law
• Human reproductive cloning	Prohibited.	Prohibited.
• Therapeutic cloning (creation of cloned embryos) Prohibited.	Allowed.	Prohibited.
Others • Surrogate mother	Prohibition of profit-making mediator's business.	Prohibited (indirectly) in the society's notice; under consideration by the government.
• Provision of embryo to other couple.	Allowed.	Under consideration.

*: The law concerning regulation relating to human cloning techniques and other similar techniques

Figure 2: Establishment of the social system for human embryos in the UK



VLA: Voluntary Licensing Authority for human in vitro fertilisation and embryology
ILA: Involuntary Licensing Authority for human in vitro fertilisation and embryology
HFEA: Human Fertilisation and Embryology Authority
HFEAct: Human Fertilisation and Embryology Act

organization designated by law (similar to an independent administrative commission in Japan). The method for deciding on bills used at the establishment of the system in the UK, i.e., the process for establishing a new social and legal regulation, may be summarized as shown below.

(i) Consideration at the advisory committee and publication of the report.
(ii) Presentation of the Green Paper (referred to as the consultation paper; it states the background of the problem, the points, and choices of a solution to make an appeal to society).
(iii) Presentation of the White Paper (framework for legislation; proposal as a bill after receiving responses to the Green Paper and arranging for considered points).
(iv) Establishment of the law at the Parliament.

A series of the process for deciding on a bill from causing the social disputes first to adopt the responses is the general method that has been conducted traditionally in the UK. The consideration of the bill related to human embryo was conducted through the same process.

3.2.2 Change of the control organization

The Report from the government inquiry into human fertilisation and embryology (referred to as the Warnock Report) in 1984*[9]. The Warnock Report made recommendations concerning: (i) licensing authority and its function; (ii) principles related to the implementation; (iii) provision for sterility therapy service; (iv) legal regulation of related research; and (v) amendment to the existing law regarding new science technology. The most important point in the report is that it stipulates a licensing organization designated by law to socially manage (control) human embryo research activities and assisted reproductive medicine*[10].

After the report, in 1985, the Medical Research Council (MRC), a body promoting medical research and related sciences, founded a voluntary licensing authority (VLA) for human *in vitro* fertilization (IVF) in collaboration with the Royal College of Obstetrician & Gynecologist (RCOG), which coordinates obstetricians and gynecologists in the UK, thereby establishing the fundamental skeleton of the current control organization's function and system.

As a background to the establishment of VLA, it was reported that a situation had developed because the government had not dealt with this matter immediately, and that there were circumstances in which control based on standards was required to avoid lawsuits from a clinical position when conducting sterility therapy. VLA was based on the recommendations of the Warnock Report, which required: (i) deciding on the code of practice; (ii) licensing of human embryo research and assisted reproductive medicine; (iii) grant review; (iv) reporting to MRC/RCOG; (v) disclosure of information related to the practice; and (vi) contributions to measures for social arguments and control procedures. Therefore, the current function of the control organization already included a major part of the recommendations. The VLA published reports annually in an effort to disclosure information.

However, by the nature of VLA, individual licensing and code of practice were dependent on voluntary participation, and its social position was different from the current Human Fertilisation and Embryology Authority (HFEA) mentioned later, which is an independent, national control organization with a compelling force.

The VLA changed its name to the involuntary licensing authority (ILA) for human *in vitro* fertilisation and embryology in 1989. To deal with the circumstance in which the RCOG stopped financial support due to monetary difficulties and the remaining MRC began receiving government allocated assistance, the VLA, in an effort to urge the government to act, emphasized through its name that the VLA was a tentative organization until the government formed a statutory organization.

With such a background, through the establishment of the Human Fertilisation and Embryology Act (HFEAct) in 1990, the control organization HFEA was founded and started activities in August 1991.

3.3 Establishment of HFEAct for the handling of human embryo and the following movements

3.3.1 From the Warnock Report to today

After the Warnock Report was published in 1984, individual views and reports on the subject of human embryo were announced by specialists' groups such as British Medical Association, RCOG and MRC, and religious groups such as the Roman Catholic Church, and researchers reportedly conducted a campaign*[11]. Taking this opportunity, the government caused arguments by the green paper in 1986, and after receiving the responses, they asked people's opinions by presenting a framework of legislation in the white paper in 1987, and a law was established at the Parliament in 1990. The skeleton of the established law, HFEAct, is (1) regulations of prohibited matters and punishment, and (2) establishment of a special control organization and regulations on the function.

At the time point of the establishment of HFEAct, the systematic foundation related to the handling of human embryo was prepared. However, science technology always continues to progress. After the establishment of the law, researches in the fields of regenerative medicine and gene therapy progressed remarkably, and in 1998, recommendations (Human Genetics Advisory Commission and HFEA) were made considering the progress during this. In 1999, a committee was organized under the Chief Medical Officer, and a recommendation regarding measures to deal with the change of science technology was made. Based on the recommendation, in 2001, Human Fertilisation and Embryology (Research Purpose) Regulations were established to add (i) increasing knowledge about the development of embryos, (ii) increasing knowledge about serious diseases, or (iii) enabling any such knowledge to be applied in developing treatments for serious diseases. In the same year, the Human Reproductive Cloning Act 2001 was established to prohibit the preparation of reproductive cloning that produces human cloned individuals (therapeutic cloning: preparation of cloned embryos was non prohibited) and provided for punishments.

With the expansion of the use of embryos for research purpose, there was a new movement. For human fertilized embryo and cloned embryo, the House of Lords select committee that conducted a positive verification regarding the actual status of use for researches compiled a report on stem cell research in February 2002. The report refers to 27 items including continuation of the use of human embryo and cloned embryo within 14 days, and the idea of setting up a stem cell bank*[12]. Complying with the recommendation, the Department of Health published a report on the measures to deal with this in July 2002. The report gives a conclusion almost in accordance with the House of Lords select committee report, and the department had conducted individual investigations of the items shown by the committee and gave their opinion on measures to deal with them in the report.

3.3.2 Current status of regulation

As the general situation of human embryos in the UK, the permit (license) system for preparation and use of human embryos and prohibition of the use after appearance of the primitive streak may be given*[13]. The prohibited matters related to human embryos in the UK are: first of all, (1) creation, storage and use of human embryos are prohibited except for creation or use under permit (license). (2) What can be transplanted to humans should be a human embryo or gamete (sperm and egg), and the use after appearance of a primitive streak is prohibited. The primitive streak, which is the first characteristic change observed in the embryo, is formed when the embryonic end in one direction is raised on the 14th or 15th day after fertilization. The separation of uniovular twin occurs until this time at latest. Based on the primitive streak, a medullary groove is formed up to 17th day, and up to around 23rd day, the bilateral structure referred to as neural folds is fused, and "spinal cord (neural tube)" comes to be observed. At the same time, in the law, from a practical point of view, the corresponding time (to use human embryos for research) is provided as "embryo not later than the end of the period of 14 days" (after gametes are

mixed). As prohibited matters, transplant of human embryo to animals is prohibited, and nucleus transplant to embryo is prohibited. In addition, for gametes, (3) it is prohibited to conduct the storage of gametes, artificial insemination, and cross-fertilization with animals without permission.

The ES cells are often established 4–5 days after fertilization, and, as such, are not prohibited. Preparation of human embryos and cloned embryos for research purpose is permitted, but preparation of cloned individuals is prohibited. For the prohibited matters, punishments are imposed, and imprisonment for a term not exceeding 10 years or a fine or both, are imposed.

On the other hand, in Japan, preparation of cloned embryos is prohibited by the law ("guideline for handling of specific embryos" based on it), and for creation of human embryos for research purpose, there are different opinions in the arguments.

3.4 Public control organization HFEA

HFEA is a public organization under the control of the Department of Health, and one of the characteristics is its high independence secured. The function and the placement in the administrative organization are regarded to be corresponding to the independent administrative committee in Japan (administrative committee with independence based on Article 3 of the National Government Organization Law). That is, HFEA is (usually) placed as an extra-ministerial department of the department, and an administrative organization that functions independently. For example, the Japan Fair Trade Commission of the Ministry of Public Management, Home Affairs, Posts and Telecommunications corresponds to this.

3.4.1 Summary of functions

Major functions are as shown below.

(1) Granting a license to institutions conducting the assisted reproductive medicine and human embryo research, and inspections.
(2) To produce a Code of Practice.
(3) Control of storage of gametes.
(4) To keep a formal register of information related to the practice.
(5) Publicity work and information supply activity.
(6) Assistance in deciding on administrative measures, etc.

3.4.2 Composition

Twenty-one committee members including the chair, and 4 senior staff and 1 observer from the Department of Health share the duties of 7 departments (committees and work sections) with the respective functions. The committees of HFEA include (i) Audit Committee, (ii) Code of Practice Committee, and (iii) Licensing & Fees Committee, etc., and they work independently, respectively. To the persons including the committee members, other research staffs are added, and the total number of the personnel in the HFEA's Executive is 45. The scale of budget for fiscal 2001 was about 2,880,000 pounds (about 550,000,000 yen). One half of this is covered by the license fees, and the other half is covered by the budget of the Department of Health. The expenditure included human expenses 1,360,000 pounds and operational expenses 1,310,000 pounds, etc.

3.4.3 License

As of 2002, 115 institutions were registered centering on institutions practicing the assisted reproductive medicine. The institutions practicing *in vitro* fertilization (IVF) were 75 institutions, and those practicing only artificial insemination were 23, and those practicing only researches were 6. The annual number of IVF practiced was 25,273 cycles, and there were 5,513 births.

The license system is associated with the obligation of detailed reporting and the inspection system. In the license system, some clinics are judged as unlicensed, or occasionally the license may be revoked. Therefore, for the practice of assisted reproductive medicine, occasionally there are some cases of lawsuits due to the license, and due to the supervising right of HFEA regarding whether it is appropriate or not to practice the assisted medicine. Of unlicensed clinics or clinics whose license in the UK was revoked, some were reported to have moved, for example, to the US to start practice. In such a sense, the technical level

as clinics has been maintained in the UK considering patients first. As for the number of revocations, two were reported in the first 9 years (Brinsden, 2000).

Based on data information obtained from practicing institutions, a guidebook for patients who receive the assisted reproductive medicine, The Patients' Guide to IVF Clinics Provisional Data 2002 presenting detailed and specific up-to-date data in each medical institution was prepared to provide data. The therapeutic results and the number of patients are easily available from this.

As stated above, HFEA is securing the quality level of human embryo-related medical care and research through the license system and the information supply to patients.

Meanwhile, a research subject applied to HFEA is submitted after being reviewed first by an institution outside of the institutions conducting the research, an ethics committee (for example, a public ethics committee LREC: the UK has an independent system of ethics review and advisory organization called Research Ethics Committees (REC) under the control of NHS of the Department of Health. In the system, LREC is the organization located for each area.). At the HFEA, after the research subject is reviewed by specialists, it is reviewed at the committee meeting*[14]. Since 1991, of 141 subjects submitted, 136 subjects were permitted, and 77 of them were already completed. As of August 2002, 28 research subjects were being conducted at 19 institutions. Major contents of the subjects are related to the assisted reproductive medicine. As for ES cells, from human embryo to the establishment of the cells is a scope supervised by HFEA, but the supervision is not extended to the use of the cells after they are established once. At present, a stem cell bank is being planned by MRC. In 2002, two plans of ES cell establishment were permitted. The reference data on the actual use of embryos are shown below.

Reference data:

Statistics on the use of human embryos from the UK between 1991 and 1999 (Walters, 2002).

(i) No. of embryos created:	925,747
(ii) No. of embryos transferred:	423,153
(iii)No. of embryos stored for own treatment:	225,627
(iv)No. of embryos stored for treatment of others:	448
(v) No. of embryos given to research:	53,497
(vi)No. of embryos discarded :	294,584
(vii)No. of embryos created for research purposes:	118

(The data are based on the HFEA annual report and the House of Lords select committee report on stem cell research.)

3.4.4 Inspection

In the inspection of a practicing institution, an inspection team is usually chaired by an HFEA member and includes a clinician, a scientist, a person with a background in another field (such as counselling or nursing) and a member of the HFEA's executive staff. The main activity of the inspection team is to visit the institution unannounced. To organize such a team, HFEA currently employs 52 part-time inspectors. An inspection protocol for the inspecting procedures was prepared and being used with occasional revisions as needed. Such a practical inspection was not the first one in the UK, and in the investigation of experimental animals conducted from a viewpoint of protection of animals from harm under the control of the Home Office, the same method was used, i.e., investigators inspected the institution without prior notice.

3.4.5 Renewal of the license

The license had been renewed every year before, but at present, for institutions with achievements, it was changed to be renewed every 3 years. In addition to the conventional inspective investigation conducted every 3 years for the license review, a small investigation referred to as an interim inspection is conducted for important items only based on the previous investigation (by the same method as that in the main investigation).

3.4.6 Code of Practice

HFEA produces the required code of practice

based on the HFEAct, which provides guidance for clinicians and researchers on the practical procedures in carrying out their licensed activities. What is regarded as particularly important in the basic concept of the code of practice is the role to protect the "welfare of a child who may be born." The code of practice provides for; (i) guidance on the proper conduct of activities of those who are licensed, (ii) standards for the materials and facilities, (iii) welfare of the child, (iv) selection and screening of donors, (v) confidentiality, (vi) provision of information, (vii) consent, (viii) offering of counseling, (ix) use of gametes and embryos, (x) storage and handling of gametes and embryos, (xi) standards and prohibitions in researches, (xii) records, and (xiii) filing of complaints, respectively.

The code of practice is decided on by HFEA, and goes into effect with the approval of the concerned secretary of state. The currently used one is the fifth edition, and the sixth one will be issued within the year 2003.

3.4.7 Pursuit of transparency

HFEA is always making an effort to increase the transparency to the society. Particularly, the thorough publicity work on the status of activities and the status of finance, and information obtained in the control is attempted. This is indicated in the reports consisting of detailed and specific descriptions (HFEA, Eleventh Annual Report and Accounts 2002).

3.4.8 Maintenance of independence

HFEA requires approval of the Secretary of State for the code of practice, and has an obligation to report to the Secretary of State. However, in the function, deliberations and decision, HFEA is said to be keeping the independence from the Department of Health and specialists' groups such as RCOG. The relationship between the Department of Health and HFEA is said to be a good "liaison" relationship, in which both always contact each other and work in close cooperation with each other. However, in the aspect of budgets, it was reported that there was friction between both.

3.4.9 Recruitment of committee members by public advertisements

The employment of committee members and staff of the HFEA including the chair was conducted through public advertisements, and it was announced that the equal opportunity was respected with elimination of every discrimination and prejudice. The applicants were recruited for the posts by public advertisements on the newspaper, etc., and selected through an interview by 3 persons, i.e., the chair of HFEA, one of the HFEA members, and a person in charge from the Department of Health. For example, there were 339 applicants for posts of 4 members, and this indicates the high level of social interest and appreciation of the duties of HFEA.

3.4.10 Specialists and general citizens

Without cooperation of specialists, it is impossible to understand and grasp professional matters appropriately, and without participation of general citizens, the social self-decision cannot be established. In the resolution of bioethical issue, mutual cooperation of specialists and general citizens is considered to be essential.

At the HFEA, the chair and the vice-chair require to be non-specialists (not a clinician, a person engaged in assisted reproductive medicine, or a researcher to obtain the grant), and the percentage of specialists in the committee was prescribed to be controlled as one third to one half of that of non-specialists. Besides, the members including the chair are recruited by public advertisements as shown above.

In the process of deciding on the code of practice and implementation of the inspection, the specialists are essential. However, the main axis of HFEA is not only to have specialists' assistance and criteria of technological judgement but also to have a viewpoint to embody the social judgement taking into account the general citizens' opinion and standpoint. This may have made it possible that the control system in the UK achieved the social trust.

3.4.11 Evaluation of HFEA

According to the comprehensive evaluation of HFEA by people concerned, the HFEA is working very effectively, though not completely. In such a

circumstance, it is obvious that researches should be conducted in a situation that science and technology are socially accepted (social persuasion and social self-decision), and researchers who are controlled understand that understand the necessity of procedures associated with this. Particularly, for researches using the national budget, the above is recognized as natural in the relationship with taxpayers.

However, on the other hand, HFEA is exposed to social indictment. For example, there was a medical mistake at a clinic where a black child was born to a white couple due to transplantation of a wrong embryo by mistake, and the HFEA was called to account for the medical mistake. As another recent example, when a couple having a child with a genetic blood disease called thalassemia were expecting their second child, they received a pre-implantation genetic test to select an embryo, and as a result, a healthy child was born. In addition, the couple planned to use the newborn's cord blood for treatment of their first child. The HFEA approved the plan, but a Catholic pressure group named Comment on Reproductive Ethics (CORE) indicted HFEA for the approval. As a result of the struggle in the courts, HFEA lost the suit, and the plan was prohibited (BBC News World Edition on Dec. 20, 2002).

3.5 Background of establishment of human embryo control system in the UK

At present, in the UK, it is said difficult to grasp the cultural and religious background as a stereotype (increased religious diversity, bipolarization of the educational level, high or low). However, in the agreement of social regulations, it is possible to indicate the presence of strict pragmatism as shown below.

(1) Stance related to the formation of social arguments

It is not realistic to expect that all of the general public should have a deep knowledge and interest in the issue disputed and the point. However, it is important to release information at least to interested people to hear their opinion thoroughly, and give them opportunities to have a discussion, and a mechanism to secure the transparency in the implementation of the system should be created.

(2) Stance related to ethics and social regulations

In the society of liberalism, the existence of the individual personal ethical sense is allowed. Then, in any agreement of social regulations, complete ethical agreement is difficult. Therefore, the major premise made is that it is natural that there is a certain degree of gap between the personal ethical sense and the social regulation and control system. On the premise, an ethical discussion is made to minimize the sum of the social gap. In addition, from the premise, measures to set up a very effective control system and secure the transparency in the system and realize participation of citizens may be adopted.

(3) Stance to the uncertainty of science technology

It is considered inevitable that the uncertainty (possibility of an unexpectable risk) exists in application of new science technology. Therefore, it is always demanded to make a judgement and a self-decision always weighing the risk and benefit ratio, and it is considered important for the society to make a situation in which such a self-decision is possible (a discussion on the degree of the uncertainty and a discussion to clarify it are not made throughout to the end).

In the background of the system in the UK, there may be a formation of social structure that can realize the consciousness of rights and methodology rooted in the pragmatism, while it is a society of individualism and liberalism with a long tradition. In the UK, to meet the social demand, the human embryo-related control system can immediately stop the research without adding a new legal regulation, as authority of the control organization (HFEA can immediately suspend the license based on a reasonable ground). In that sense, the system in the UK may be said to be a system possible to take quick and flexible measures to meet social demands, differing from the US without federal legal regulations on the assisted reproductive medicine and general researches of human embryo and

Japan only depending on self-imposed regulations on them. Needless to say the foundation of such quick and flexible measures exists in the comprehensive function of the control system in the UK including the inspection that can grasp the actual status of the implementation of human embryo research and assisted reproductive medicine. With the uncertainly contained, such a system possible to take flexible measures is considered to be important as a foundation or background to appropriately implement and develop the life science technology attempting the social acceptance as well.

As opportunity to have a direct discussion between the general society and proposers of the measures, a sex selection debate was held, and here we introduce the discussion as one sample of the discussion between them.

First, HFEA published a booklet (called a consultation document) compiled to cause disputes in the general society. Making this a common basis, a few dozen of general participants who got together in a corner (Jubilee Room) of the House of Commons and several panelists of specialists including the chair of HFEA had a discussion to directly talk with each other. In the discussion, there were some participants from the pressure group opposed to the HFEA, and occasionally a considerably hot discussion was made. After the discussion, the participants had an informal talk over light meals at the site, and interested persons had a discussion with each other.

In the issue of sex selection, the main point is whether its general application is approved or not besides medical reasons. In addition to various social issues related to sex differences, whether it is right or wrong that the acceptance of sex selection may lead to selection or preparation of born children with characters that the parents want by the genetic diagnosis or modification (as the door to a designer baby) is being discussed.

As stated above, in the relationship with the general society, (i) information supply from the professional organization, (ii) direct exchange of opinions and discussions, and (iii) mutual understanding through them and adopting opinions from the general society are conducted.

We can say that the discussion between the general citizens and specialists is an example contributing to the formation of the basis of mutual understanding (sharing of information and knowledge) when the control organization and the general society solve a problem collaboratively.

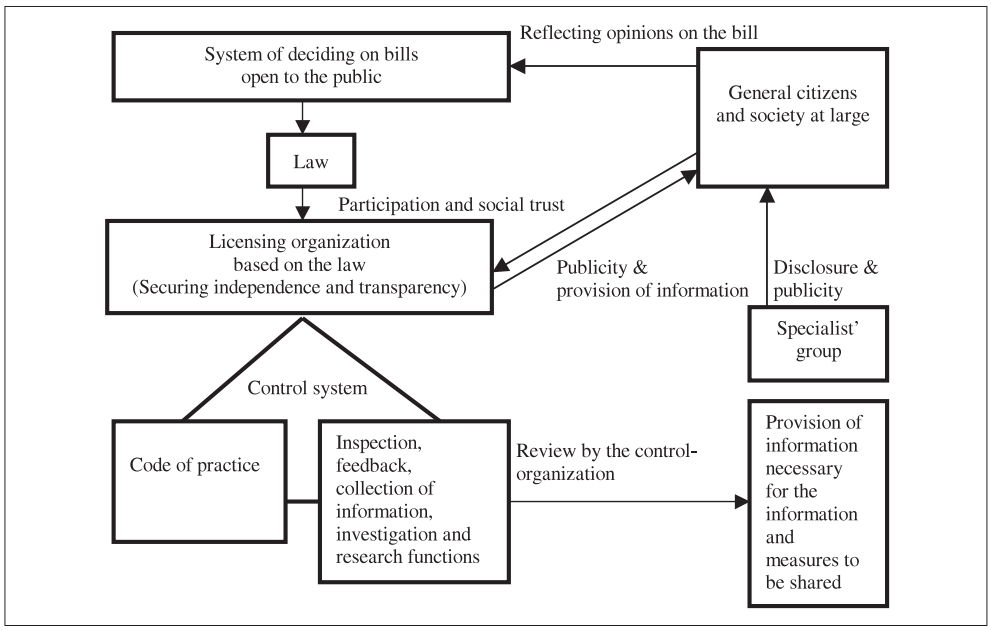
3.6 Conclusion–Consideration of a system construction in Japan

It is possible to grasp the elements of the system in the UK, based on their interrelationship as shown in Figure 3.

Firstly, in this system, the organization set up by law decides on the code of practice from a professional point of view. The code of practice itself has no binding force associated with punishments. However, at the licensing, the status of the practice is evaluated from the viewpoint of the code of practice, and if there is any inappropriate deviation, the license is revoked. Conversely, when the status related to the practice changed with the progress of life science technology, even if it is a method not necessarily meeting the code of practice, if its validity was confirmed, the method can be approved by judgement of the committee.

That is, for the code of practice showing practical procedures, if more developing method was established with the progress of life science technology, the new method can be adopted without adopting the code. The validity is judged by the committee at the licensing, and if the new method was appropriate, it will possibly be approved. Unlike law, the code of practice can be revised by the committee permanently set up in the control organization, and it is easy to take appropriate measures at the present time including the social acceptance. That is, the flexibility and adaptability to deal with a new problem, which are important characteristics of the system in the UK, are based on the functional liaison between the licensing organization and the code of practice decided on by the licensing organization. An important function to support the evaluation in such a licensing is considered to be the inspective investigation, and the function is conducted by the method that becomes effective

Figure 3: Analysis of the system structure in the UK



by the control organization.

Secondly, the important point is to be careful about securing the independence and transparency of the professional control organization, and to conduct deliberations of the licensing by a committee meeting established by participation of both general citizens and specialists. As a result, the committee can make a judgement from a viewpoint of the general society, and it becomes possible to avoid the separation of the judgement at the control organization from the social acceptance, and it may lead to that the social trust of the control organization can be obtained.

Thirdly, the professional control organization has an investigation and research functions. The function makes appropriate advice related to measures, and information supply and publicity work possible. That is, it makes it possible to share the information to be a basis of judgement at the committee of the control organization and information to decide on the related bill among the people concerned, specialists and the general society. In other words, appropriate information can be supplied not only to the committee of the control organization but also to the social discussion and the discussion at the site of deciding policies. The review (for example, consultation document on a specific problem) issued by the UK's control organization HFEA has very high quality contents. The high level of the control organization that can issue such a review can increase the reliability in the general society, and is presumed to be reflected to the high level of measures. Besides, with the accumulation of information at the professional control organization, that it is possible to develop the ability of the investigative research function itself more getting new information continuously may be important as a basis to deal with the development of life science technology in the future.

In addition to the construction of such a system, the organization to practice and researchers should understand the significance of social acceptance in the progress of science technology and accept the social control system. It is expected that specialists' groups do not remain in their private position and are involved in public measures voluntarily, and it is also expected that members of the general society are positively involved in the formation of public measures as formers of a community, and it is important that the opportunity and process for discussions and hearing for that are set up.

As for the uncertainty contained in the state-of-the-art life science technology, as the research develops, the actual status and the practical influence become visible. Besides, new science technology appears one after another. Then, a static regulation only by law has its limitation. On the aspect of life science technology changing all the time, and on the aspect of the society that accepts it, a dynamic and comprehensive control

system works to deal with them appropriately, and the development of life science technology and the social acceptance must be obtained at the same time. The system in the UK is considered to be clearly suggesting what kind of social governance system is required in Japan.

How the respective countries deal with common social questions (ethical questions of science technology) raised by life science technology developing rapidly will have a significant influence on the future world. However, as seen in the questions raised by the state of the social regulation of bioethical issues, at present in Japan, (i) we can say that the social technology forming the social system to adapt to changes and the basic structure to give dynamism to various systems constituting the society are still poor or fragile. In addition, (ii) we can indicate that the system to realize and operate the community to flexibly adopt the social voluntary participation and social opinions and discussions is not enough partly. Therefore, the general citizens, specialists' groups and government must collaboratively aim to realize the practice of researches and medical care and the social acceptance at the same time.

In the future, the bioethical issues induced by the progress of life science technology are considered to be increased and more serious, and to resolve them, it may be the time for Japan to aim at constructing a social governance system (control system based on the social self-decision) of life science technology. When we construct a system that conforms to Japan, it is effective to refer to the state of the existing system in the UK constructed reasonably. That is, what we have to consider is setting up an independent committee that controls bioethical issues, and constructing an organization to solve problems professionally based on the licensing system, and the system. With such a system as a skeleton, the basis to deepen the arguments of bioethical issues in the society and the basis of the transparency and disclosure are likely to be formed.

In the US where there is no professional control organization established similarly to Japan, there was an opinion that the necessity of setting up a professional control organization for the current life science technology was the same as the necessity of setting up the Federal Aviation Administration to deal with the civil aviation services that had just appeared. This indicates that the new aspect of the modern life science technology is already in a situation difficult to control as science technology of new age without a professional organization (Fukuyama, 2002).

For Japan aiming at a nation based on science technology and invention, the touchstone for future prospects of science technology and social system in Japan may be unexpectedly found in such a point (how to tackle the construction of a social system to deal with the bioethical issues).

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Glossary

* 1 The clone law and arguments at the Council for Science and Technology Policy (Expert Panel on Bioethics)

The clone law, "The Law Concerning Regulation Relating to Human Cloning Techniques and Other Similar Techniques" (2000), was provided mainly to prohibit preparation of human cloned individuals. Article 2 of the supplementary provisions provides "within three years of this Law, take necessary measures in accordance with the results of the study and examination by the Council for Science and Technology Policy, Cabinet Office concerning the method of handling of a human fertilized embryo as the beginning of a human life" and the time limit is June 2004.

The assisted reproductive medicine is being

conducted in at least 36 countries as sterility therapy (Suganuma, 2001; pp. 152-161), and the criteria provided individually are used in the respective countries. However, a standardized regulation is being sought out by EU (European Group on Ethics in Science and New Technology).

* 2 Regenerative medicine and ES cells

"Regenerative medicine" is to positively utilize cells of biological tissues or organs that caused functional disorder or dysfunction to attempt regeneration of the functions (The Japanese Society for Regenerative Medicine). As cells expected to support such a medicine, cells having proliferative ability (and autoproductivity) and differentiating ability, that is, cells called stem cells attract attention.

The stem cells consist of embryonic stem (ES) cells established from early embryo, fetal tissue stem cells and EG cells established from fetal germ tissues, and somatic stem cells possible to be collected from adults. In relation to human embryos, particularly, establishment of ES cells is the question.

The property of ES cells is that they have a latent ability that may contribute to formation of every organ, and that they have a good proliferative ability and a great deal of experience in animal experiments and are considered to be easy to establish a culture system maintaining the character stably. As for somatic stem cells, one type with a good differentiating ability was reported, but the difficulty in their collection and growth in the culture system is indicated.

* 3 Change of the regulation of human embryo

In Germany, "the law of embryo protection" was established in 1991, and the use of human embryos was strictly restricted, although the assisted reproductive medicine was allowed. However, according to "the stem cell law" (Gesetz zur Sicherstellung des Embryonenschutz im Zusammenhang mit Einfur und Verwendung menschlicher embryonaler Stamzellen) proclaimed on June 28, 2002 (enforced on July 1), as an exceptional provision, the import and use of ES cells for researches were to be allowed conditionally (Iwashi, 2002). In the UK, in 2001, the text of the law was added to approve expansion of the use for researches.

* 4 Regulation in Japan and the issues

In our country to date, no law including comprehensive and direct provisions on the handling of human embryos has been established. The Japan Society of Obstetrics and Gynecology has established rules as the society's notice to apply them to the assisted reproductive medicine and researches conducted by the members. However, it is in a state of voluntary and arbitrary one limited to the members registered at the society.

On the other hand, there are various issues including the current status that occasional acts contrary to the self-imposed restraint of the society's notice are performed openly, appearance of the new concept of giving priority to children's welfare such as the right to know their birth details and parentage, demands of mental support by counseling, and complicated genetic and social mother-and-child relationship related to surrogate mother, embryo provision, and artificial insemination and concern about the influence on the legal system and social system. With the question about whether the assisted reproductive medicine between non-spouses is right or wrong including all the above issues, discussions considering the legislation are being conducted centering in an investigational committee at the Ministry of Health, Labour and Welfare (Assisted Reproductive Medicine Section, Health and Science Council). However, the assisted reproductive medicine between spouses remains to be left without particular control, regulation and protection of the government.

* 5 Progress of life science technology and bioethics

In March 2001, in the "Science and Technology Basic Plan" for the second term, life science was given as one of four fields regarded as important, and in the item of "Science technology-related ethics and social responsibility," the significance of the issue of bioethics as a subject inseparable from the development of science technology was listed first.

* 6 Sociological consideration as part of life science technology

In the US, research programs of Ethical, Legal and Social Issues (ELSI) were started in 1990. The purpose is to specify the ethical, legal and social issues associated with the human genome plan and genome researches, and analyze them, and provide information about the issues to the general society. The research programs are used by the National Human Genome Research Institute (NHGRI) of NIH and the Office of Biological and Environmental Research (OBER) of the Department of Energy. By the authorities, at least 284 research and education programs were supported, and more than 625 achievements were reportedly made. The achievements were evaluated to be an important intellectual foundation of bioethics-related policies. EU appropriate 2% of the budget of science research grant-in-aid for ethical researches (Ayano, 2001). The Japan Association of Bioindustries Executives, 2001.

* 7 *In vitro* fertilization (IVF) children

Patric Steptoe and Robert Edwards, whose study succeeded in the birth of the first IVF child, reportedly could not get public research expenses because of doubts in safety (J. Gunning).

In Japan, the birth of the first IVF child was reported by Tohoku University in 1983, and ethical disputes were caused, and at the same time, many inquiries from people suffering from sterility were reportedly received at the Department of Obstetrics and Gynecology of the university (Suganuma, 2001, as citation from Suzuki, M.: "*In Vitro* Fertilization: Documentary to the success," Kyoritsu Shuppan, 1983).

In Japan, there were reportedly 12 thousand cases of IVF children (approx. 1% of all newborns, 2000) annually, and more than 40 thousand cases in cumulative total (Council for Science and Technology Policy, 2001; Suganuma, 2001, pp. 72–82).

* 8 Human cloning

Currently, international cooperation of human cloning regulation, that is, an international treaty for prohibition of human cloning is being assessed in the United Nations (proposed by Germany and France at the 56th general assembly on August 7, 2001). However, some countries are appealing for prohibition of both reproductive cloning and therapeutic cloning centering in the US, and other countries are appealing for prohibition of reproductive cloning first of all (e.g., Germany, France, Japan), and the difference in opinions between both has not necessarily been ironed out (Hishiyama, 2002).

* 9 Details leading to the Warnock Report and HFEAct

For the details leading to the Warnock Report and HFEAct, Miki (1995) analyzed them as shown below.

The Departmental committee on Human Artificial Insemination, which was set up within the government office in 1958, issued a report in 1960. In the report, they approved artificial insemination with husband (AIH), and stated that they did not regulate artificial insemination with donor (AID) but would not use it as far as possible. After that, in 1973, a committee set up in the British Medical Association made a proposal, and based on the proposal, the self-imposed restraint by the Royal College of Obstetrician & Gynecologist (RCOG), establishment of the AID center, and application of the National Health Service were realized. At this point of time, artificial insemination is considered to have been accepted as a technique socially insuppressible.

* 10 Warnock Report

The Warnock committee was organized as an advisory committee by the government in 1982.

• The composition of the members is: philosophy 1, theology 1, administration 1, midwife 1, clinician 3, psychology 2, medical research 1, head of review board 1, social worker 1, lawyer 2, foster parent association 1, chairman of foundation 1, a total of 16 members.

• Collection of opinions: testimonies of 254 groups, 695 letters remitted.

• Subjects discussed: (a) common issues, (b) individual issues ((i)artificial insemination, (ii)

in vitro fertilization, (iii) offer of egg, (iv) offering method of embryo, (v) surrogate mother, (vi) application of the technique of sterility therapy, (vii) freezing and storage of semen, egg, and embryo), (c) research of various problems in scientific research and the prospects, (d) contraceptive treatment service and regulation of research.

• The composition of each subject was to be: (1) definitions and contents, (2) objections, (3) favorable opinions, (4) view as the advisory committee and the matters to be noted.

• As for the conversion of opinions, it conversed in all items except for the item of use of embryo. Issues with different opinions were described at the end of the article as "expression of different opinions."

* 11 Social responses after Warnock Report

Many mass media took up the report in the society, and in 1985, it was reportedly agreed that the issue is a social problem requiring a careful consideration (Muto, 1994). As a result of a sufficient campaign, general people's interest was caused, and the human embryo-related knowledge, for example, even what "the primitive streak" was said to have spread in those days (A. McLaren).

In the health system in the UK, the order of priority in the fund supply of the National Health Service (NHS) by disease is decided by the local authorities, but the order of priority in assisted reproductive medicine is not high (said to be after treatment for erasing tattoos). The fund is only received for about 20% of the assisted reproductive medicine, and there are some conditions in the fund supply, and it is reported that there is a waiting list of about 4 years (Ishii, 2001b).

* 12 House of Lords select committee on stem cell research report

Considering the expansion of researches using embryo in 2001, a positive investigation of the actual use for research purpose was conducted to report. For the investigation, testimonies were obtained from 53 associations and 58 persons in writing or in writing and orally, respectively, to make them grounds for judgement.

The principal points of the investigation were: (i) the point that use of embryo may be unnecessary because of the progress of somatic stem cell researches, (ii) the point that use of embryo is expanded to the research purpose may be ethically inappropriate, and (iii) the point that the use may lead to preparation of cloned individuals. For these points, recommendations covering 27 items were made, and a summary or copy of the major items is shown below. (The figures are the numbers specified in the report.)

4. To ensure maximum medical benefits, it is at present necessary to keep open both routes (ES cells and somatic stem cells) in therapy, since neither alone is likely to meet all therapeutic needs.
7. Whilst respecting the deeply held views of those who regard any research involving the destruction of a human embryo as wrong and having carefully weighed the ethical arguments, the Committee is not persuaded, especially in the context of the current law and social attitudes, that all research on early human embryos should be prohibited.
8. Fourteen days should remain the limit for research on early embryos.
9. Embryos should not be created specifically for research purposes, unless there is a demonstrable and exceptional need that cannot be met by the use of surplus embryos.
11. With regard to the rule of embryos for research purposes within 14 days, ethically, fertilized embryos are not distinguished from cloned embryos.
12. Cloned embryos should not be prepared unless there is sufficient reason that surplus embryos are inappropriate for a specific purpose.
14. Due to the problem of safety, preparation of human cloned individuals cannot be approved at this stage.
15. From an ethical point of view and due to problems involving human experiments and the welfare of the family and children, etc., preparation of human cloned indi-

viduals cannot be permitted.

19. In light of the progress of somatic stem cell researches, etc., whether human embryo researches are still required or not should be judged at an appropriate time, perhaps towards the end of the decade.
23. When the Government brings forward legislation, consideration should be given to making an express provision for such basic research when necessary as a precursor for the development of cell-based therapies.
24. The condition of offering sperm and egg free of charge is important for preventing commercialization of assisted reproductive medicine, and should be strictly maintained.
26. It is necessary to establish a stem cell bank under a committee for supervision and direction in order to verify the quality of ES cells and to monitor the use, and the ES cells for research licensed by HFEA should be registered there.
27. Considering well the characteristics of ES cells that enable permanent subculture, HFEA should make it mandatory to obtain informed consent for such use including for various situations in the future. If the range of use is limited in the first informed consent, ES cells should not be established using an embryo.

* 13 Primitive streak

Since Warnock Report, in the UK, based on the developmental change, the appearance of "primitive streak" has been used as an aim of one section in the development from embryo to individual.

Reference:

In Germany, the process after fertilisation to the time point of nuclear fusion is not regarded as a human embryo to be protected. It is because after fertilization, two pronuclei originated from the sperm and egg, respectively, exist separately for about 12-24 hours to cause DNA replication, and after completion of the replication, nuclear membrane is fused and synapses of chromosomes occur first, when the maturity as a single cell is completed. During the time, it is a stage on the way to formation of a single embryo possible to grow, that is, it was regarded as not corresponding to the concept leading to a human individual as a subject for protection. Therefore, in Germany where frozen storage of human embryo is prohibited, only fertilized eggs before nuclear fusion are considered to be subjects for procedures of researches including the freezing procedure. However, in Germany, embryo transplant, etc., in the assisted reproductive medicine is permitted. (Günther & Keller, 1991; Ichinokawa, 1994; Suzumori, 2002, p. 19.)

* 14 Review of research subject

In order to conduct a peer review (review by specialists) of the research subject, 44 peer reviewers were registered at HFEA, and the purpose of the research subject, the potential importance, the justification for use of human embryo, the validity of the experimental plan, the suitability of the duration, and the suitability of the qualification of the applicants are judged. The results of the review are shown to the applicant, and the application is revised to increase clarity and sent for license review by the HFEA committee.

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